REMARKS

This Amendment is responsive to the Office Action mailed July 13, 2007. Reconsideration and allowance of the application as here amended is requested.

The Office Action

Claims 10-23 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Cesmeli, "An Automated Temporal Alignment Technique for the Translation and Rotational Correction of Digital Radiographic Images of Bjork-Shiley Heart Valves," Proc. of Computers in Cardiology pp. 619-22 (hereinafter "Cesmeli").

Brief Review of Perfusion Imaging

The Office Action states that "image frames are taken at a speed of 15 or 30 frames per second, which means they are taken while utilizing a perfusion measurement." Office Action at pages 2-3. This statement indicates a fundamental misunderstanding regarding this term of art – perfusion imaging does not simply mean "acquiring image frames rapidly". As perfusion imaging is fundamental to the present application, a brief review of this concept is provided.

In physiology, perfusion is the process of nutritive delivery of arterial blood to a capillary bed in the biological tissue. (Wikipedia). In perfusion imaging, a contrast agent is administered to a subject, and the perfusion of the contrast agent into or out of tissue in a region of interest (ROI) is observed by a suitable imaging technique. *See* present application at ¶[0002] (Note: application references are to US 2002/0095086 A1 published July 18, 2002)

Perfusion imaging can provide quantitative information by comparison of successive images during perfusion of the contrast agent. For example, the intensity of a voxel over time during perfusion can be plotted to provide a curve whose slope, time constant, or other derivative-type parameter quantifies the rapidity or slowness of the contrast agent perfusion.

The Present Application

The present application relates to perfusion imaging, and to improved approaches for spatially aligning the images of a perfusion imaging sequence. It is useful to spatially align the images of the sequence of images so as to facilitate visual comparison across the sequence, and to ensure pixel-to-pixel or voxel-to-voxel correspondence across the sequence of images for quantitative analyses.

A usual approach for aligning a sequence of images is to align each successive image with the first image of the sequence. Since every image is aligned with a common reference image, i.e. the first image in the sequence, it might be expected that all the images would be well aligned.

As recognized in the present application (e.g., ¶[0006]), however, this may not be the case for a perfusion imaging sequence. As the contrast agent perfuses into the ROI over the course of the perfusion imaging, the contrast of the ROI can change dramatically. For example, consider a blood-borne contrast agent that darkens the intensity and perfuses into the ROI from the "left". In such a case, the ROI can be expected to begin darkening on the left while the right side initially remains unaffected. As more contrast agent perfuses into the ROI, the darkened left portion extends further into the ROI, and may eventually extend across the entire ROI. On the other hand, if perfusion is slowed or blocked in some regions, those regions may darken more slowly, or may not darken at all in the case of a complete blockage.

As a consequence, intensity or contrast features used as landmarks for the image alignment may also change drastically over the course of perfusion imaging. Features that were present in the initial images may shift or even disappear in later-acquired images due to the perfusion of contrast agent into or out of the ROI, while new features may appear in later images that were not present in the initial images. Attempting to perform image alignment employing landmarks that shift, disappear, or appear over time is problematic to say the least.

The present application discloses an elegant solution:

> An alternative version that is to be preferred, however, is characterized in that the first image in time of every pair of successive images serves as a reference base and that the subsequent second image is transformed so as to minimize differences between said second image and the reference base. This version yields a stable image in which comparatively small variations that occur during a practical perfusion measurement can be suitably tracked, so that the series of images presented for visual inspection enables very adequate analysis of the perfusion behavior of the organ being examined.

U.S. 2002/0095086 A1 at ¶[0006].

Each successive image in the sequence is aligned with the immediately preceding image, and the image so aligned serves as the reference image for alignment of the next image in the sequence.

Notice how elegantly this solves the aforementioned problem of continually shifting, disappearing, and appearing landmarks. Although the landmarks may indeed change dramatically over time, the changes in such landmarks between each image and its immediately succeeding image is expected to be relatively small. Therefore, two images adjacent in the sequence of images can be expected to have about the same intensity or contrast landmarks, and so alignment of two successive images is straightforward and is not problematic.

Moreover, since in the disclosed technique each aligned image is used as the reference image for aligning the next successive image in the perfusion sequence, any movement of the organ on a longer time scale (for example, due to a shift in the patient's position) is properly accounted for since all the image alignments are referenced back to the beginning of the sequence, through the sequence of intermediate reference images each aligned with the previous reference image.

Still further, no computational complexity is added – the same image alignment processing can be employed, but the images selected for alignment are immediately adjacent in time, rather than aligning each image with a common reference image as has been done heretofore.

The Claims Distinguish Patentably Over the References of Record

Claim 10 relates to a system for visualizing perfusion behavior of an organ, which system includes a processor programmed to, for each image in a series of images acquired in temporal succession, determine a transform that minimizes positional differences between a reference region in the immediate vicinity of the organ in each image and the same reference region in an immediately preceding image of the series of images.

As an initial point, Cesmeli does not disclose a system for visualizing perfusion behavior. The mere acquisition of images in rapid succession, i.e. 15 or 30 frames per second, does not disclose perfusion imaging. Cineangiographic imaging is disclosed in Cesmeli, but this merely denotes cine imaging for angiographic purposes. Cineangiographic imaging does commonly employ a blood-borne contrast agent, but this agent is used to provide enhanced definition of the lumen of vascular regions which, along with the cine imaging, allows for accurate imaging of changes in the heart chamber volumes and in major arterial lumens during cardiac cycling or, in the case of Cesmeli, to provide such definition for *in situ* monitoring of the performance of Bjork-Shiley heart valves. The contrast agent is not used in cineangiographic imaging to facilitate perfusion measurement.

Moreover, Cesmeli does not disclose a processor programmed to, for each image in a series of images acquired in temporal succession, determine a transform that minimizes positional differences between a reference region in the immediate vicinity of the organ in each image and the same reference region in an immediately preceding image of the series of images.

Cesmeli discloses a two-step alignment process (with some additional preprocessing including contrast enhancement, median and Gaussian filtering). The first step is translational alignment, which is performed by aligning centroids of the segmented valve images according to their principle axes. The valve contour is obtained by tracing and the valve centroid calculated, and the centroids are aligned. This step does not entail minimizing positional differences between a reference region in the immediate vicinity of an organ in each image and the same reference region in an immediately preceding image of the series of images.

The second step is rotational alignment. Casmeli expressly teaches: "The first frame of the sequence is chosen as the reference frame for rotational alignment." Casmeli p. 620, right-hand column. Rather than using the approach of claim 10, which minimizes positional differences between a reference region in the immediate vicinity of the organ in each image and the same reference region in an immediately preceding image of the series of images, Casmeli uses a single common reference image, namely the first frame of the sequence, as a common reference frame for aligning all the subsequent frames of the sequence.

This approach works fine for Casmeli, because the sequence of Casmeli is a cineangiographic sequence, and not a perfusion sequence. As a cineangiographic sequence, at most the images will differ by some relatively small shifting or rotation caused by cardiac cycling, but the landmarks used for alignment are not expected to disappear, appear, or shift dramatically.

As discussed previously, the approach of Casmeli would likely not work well for a perfusion sequence. Rather, the approach of claim 10 works well for a perfusion sequence because by minimizing positional differences respective to an immediately preceding image of the series of images it is expected that both images will have about the same intensity or contrast landmarks in spite of the dramatic changes in landmarks that may be present across the perfusion sequence as a whole.

Claim 12 has been placed into independent form including all limitations of canceled base claim 11. Claim 12 pertains to a method of visualizing perfusion behavior of an organ, and includes the operation of determining a transform that minimizes positional differences between the reference region in each image and the reference region in a preceding reference image wherein the reference image is an immediately preceding image.

Again, Casmeli does not disclose determining a transform that minimizes positional differences between the reference region in each image and the reference region in a preceding reference image wherein the reference image is an immediately preceding image. Rather, Casmeli minimizes positional differences between each image and the first image of the sequence, which is a suitable alignment procedure for the cineangiographic sequences of Casmeli but is not suitable for the dramatically changing images of the perfusion imaging sequence of claim 12.

Claim 17 depends from claim 12, and further calls for the acquiring of the series of images to include magnetic resonance imaging a subject that has been injected with a contrast liquid that facilitates perfusion measurement.

As an initial matter, it is respectfully submitted that Cesmeli does not anticipate claim 17 because Cesmeli does not entail magnetic resonance imaging. Cineangiography is generally an x-ray technique, and certainly does not inherently entail magnetic resonance imaging.

Furthermore, while cineangiography may employ a contrast liquid (i.e., contrast agent), it does not employ a contast liquid that facilitates perfusion measurement as claimed in claim 17.

Claim 21 relates to a method of visualizing perfusion behavior of an organ, the method comprising performing a transformation generation on every pair of successive images from a series of images of the organ in such a manner that subsequent to the transformation, the organ is displayed in a common position in each image, the transform operation being determined from a reference region in the immediate vicinity of the organ in the images of the series such that the perfusion behavior of the organ can be visualized while other less important parts of the images are subject to displacement from image to image.

Respectfully, nowhere does Cesmali disclose or fairly suggest performing a transformation generation on every pair of successive images from a series of images of the organ in such a manner that subsequent to the transformation, the organ is displayed in a common position in each image. Rather, Cesmali performs an independent translational alignment of the centroid of each image, and performs a rotational alignment of each image respective to the first image. Again, the approach of Cesmali works well for the cineangiographic image sequences which are the subject of Cesmali, while the wholly different method of claim 21 works well for the perfusion image sequences which are the subject of the present application.

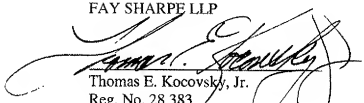
CONCLUSION

For the reasons set forth above, it is submitted that claims 10-23 distinguish patentably and unobviously over the references of record and meet all statutory requirements. An early allowance of all claims is requested.

In the event the Examiner considers personal contact advantageous to the disposition of this case, he is requested to telephone the undersigned at (216) 861-5582.

Respectfully submitted,

FAY SHARPE LLP



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